ON THE ACTION OF ACYL REAGENTS ON THE SUBSTITUTED UREAS

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B I B L I O G R A P H Y

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The object of the work described in this paper was to find out the reactions involved in the treatment of ureas and substituted ureas with acyl reagents.

In a paper*, Doctor F. B. Dains gives some interesting results obtained by the action of acid chlorides on ureas, which can be formulated as follows:

$$\text{I.-}\ (RNH)_2CO + RCoCl \rightarrow RNHCONR + HCl$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad |$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad COR$$

The acyl urea dissociates, forming an anilide compound, and an isocyanate and HCl.

$$RNHCONR + HCl \rightarrow RNHCOR + RNCO + HCl.$$
$$\quad |$$
$$\quad COR$$

$$\text{2.-}\ RNHCOR + RNCO + HCl \rightarrow RNH\diagdown \atop RN \!=\! \diagup CR.HCl + CO_2$$

The anilide and the isocyanate react at the temperature employed, giving an amidine and liberating CO_2. These amidines are aryl derivatives of $HC\overset{NH}{\underset{NH_2}{<}}$, formamidine, the simplest amidine known.

There is little doubt but that an intermediate compound is formed during the reaction, the monoacyl di aryl urea of the type $RNH\diagdown CO \atop RN\diagup COR$

Such derivatives can be obtained by the action of acids on the carbodiimides.

* Jour. Am. Chem. Soc., XXII, 181.

However, these substitution products are not stable at the temperatures employed to bring about reaction and hence they have not been isolated under these conditions.

The reactions have never gone quantitatively, according to Equation II. Some of each of the possible products have been isolated in every case. In the investigation, various temperatures have been tried in order to ascertain the conditions for obtaining the best results. Each reaction was carried on in a sealed tube and this, being heated in a bomb furnace at the required temperature until the reaction was thought to be complete.

The ureas used were all made by heating one part of pure urea with three parts of freshly distilled aniline, or the corresponding amines, on an oil bath at 160° - 170° until the odor of ammonia was gone.

$$2\ RNH_2 + \begin{matrix} NH_2 \\ NH_2 \end{matrix}\!\!>\!CO \rightarrow \begin{matrix} RNH \\ RNH \end{matrix}\!\!>\!CO + 2\ NH_3$$

These ureas were recrystallized from alcohol, benzene, or hot water, depending on which solvent gave the purest product. The acid chlorides were Kahlbaum standard reagents.

DIPHENYL UREA AND ACETYL CHLORIDE

15 grams diphenyl urea and 5 grams acetyl chloride were heated in a sealed tube at 140° - 150° for four hours. The tube opened with much pressure and HCl and CO_2 were given off. The odor of isocyanate could be noticed very

plainly. The contents of the tube dissolved in alcohol very readily. The alcohol was evaporated off and a dilute HCl solution added. The acid solution was filtered off, after allowing it to dissolve any base present in the reaction product, but, on adding NaOH to it, no base could be obtained. The black, gummy residue left was dissolved in alcohol and was found to be acetanilid. Melting point from hot water, II2° C.

Dains gives the reaction as follows:-

I.- $(C_6H_5NH)_2CO + CH_3COCl \rightarrow C_6H_5NHCOCH_3 \uparrow + C_6H_5NCO \uparrow HCl$.

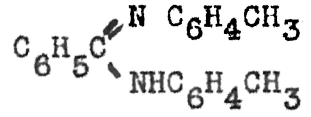
2.- C_6H_5NH \
$C_6H_5 N=C.CH_3.HCl$

He identified the base by its melting point and the analysis of the platinum salt. It is evident that my reaction did not go to completion and hence only the anilide was found.

DI-ORTHOTOLYL UREA and BENZOYL CHLORIDE

I5 grams di-orthotolylurea and I0 grams benzoyl chloride were heated at I70° to I80° in a sealed tube for four hours. The tube opened with pressure due to CO_2, Hcl and isocyanate could be noticed in the escaping gases. The contents dissolved in warm alcohol. Dilute HCl solution was added to the contents, after the alcohol had been evaporated. This clear solution dissolved out the base and, on adding NaOH to this solution, the base was precipitated. It dissolved readily in alcohol on heating and was crystal

lized from alcohol by cooling the solution in ice. Melting point, 87° to 88°. This base is diotolylbenzamidine.



$C_{21}H_{20}N_2$

It crystallized in small, white crystals. On drying the base, it was a fine white powder. It was analyzed for nitrogen by the Kjeldahl method.

0.1532 gram substance required 10.33 Cc. N/10 acid.

	Calculated for $C_{21}H_{20}N_2$	Found
Nitrogen	9.33	9.44

From the rest of the reaction product, a good yield of benzorthotoluid was obtained in fine crystals. Melting point, 131° C.

DIORTHOTOLYL UREA and ACETYL CHLORIDE.

Diorthotolyl urea and acetyl chloride were treated in a similar way to benzoyl chloride, but no base could be obtained for analysis. It must be a low melting compound, if the base is formed. The main product was acetorthotoluid*. Melting point, 110°.

DIPHENYLUREA and ISOVALERYL CHLORIDE.

10 grams dipnehylurea and 5.6 grams isovaleryl chloride were heated in a sealed tube at 140° C. for four hours. The tube opened with considerable pressure and the strong odor of isovaleryl chloride prevented any other odor being detected. The acid solution decanted from the contents

* A. 252,319.

gave a white base on adding NaOH. Melting point, 102° to 103° C. The picrate melted at 144° to 145° C. The platinum salt melted at 207° C. The platinum salt gave the following analysis:

.1126 gram platinum salt gave .0239 grams platinum.

.1103 grams platinum salt gave .0237 grams platinum.

	Calculated for $(C_{17}H_{20}N_2)_2PtCl_6$	Found
Platinum	21.35	21.22 21.49

DI-METATOLYL UREA and ISOVALERYL CHLORIDE.

10 grams di metatotyl urea and 5 grams isovaleryl chloride were heated in a sealed tube at 140° to 150° C. The contents of the tube were dissolved in alcohol and then dilute HCl was added. After evaporating off the alcohol, NaOH added to the acid solution gave a base. This base was purified from alcohol and melted at 101° to 102° C. It is a fine, white powder. No HCl salt could be obtained by saturating a benzene solution of the base with dry HCl. The platinum salt was made. Melting point, 214° C. The base was di metatolyl isovaleramidine.

$$(CH_3)_2CHCH_2C\begin{matrix}=NC_6H_4CH_3\\ \diagdown NHC_6H_4CH_3\end{matrix}$$

$C_{19}H_{24}N_2$

.2063 grams base (Kjeldahl) required 15.69 Cc. N/10 acid.

	Calculated for $C_{19}H_{24}N_2$	Found
Nitrogen	10.0%	10.64

.0642 gram platinum salt gave .0129 gram platinum.

	Calculated for $(C_{19}H_{24}N_2)_2PtCl_6$	Found
Platinum	20.07	20.09

DI-PARATOLYLUREA and ISOVALERYL CHLORIDE

20 grams di-paratolylurea and 10 grams isovaleryl chloride were heated together in a sealed tube at 150° C for four hours. The contents were dissolved in benzene and dilute HCl added in order to dissolve out any base present. NaOH was added to the acid solution and a yellow colored base was formed. This base was dissolved in alcohol and allowed to crystallize, becoming a white powder on drying. Melting point, 91° to 92° C. The HCl salt melted at 175°C. The platinum salt melted at 198° to 199° C.

ANALYSIS OF PLATINUM SALT:

.1035 gram salt gave .0209 gram platinum.

	Calculated for $(C_{19}H_{24}N_2)_2PtCl_6$	Found
Platinum	20.07	20.19

ANALYSIS OF BASE FOR NITROGEN (KJELDAHL).

.1246 gram base required 8.76 Cc. N/10 acid.

	Calculated for $(C_{19}H_{24}N_2$	Found
Nitrogen	10.00	9.86

The base is di-para-tolylisovaleramidine.

$$(CH_3)_2CH\ CH_2\ C\begin{matrix}=NC_6H_4CH_3\\ \diagdown\ NHC_6H_4CH_3\end{matrix}$$

DI-PHENYL UREA and META-NITROBENZOYL CHLORIDE

I5 grams diphenyl urea and I3.I grams meta-nitrobenzoyl chloride were heated in a sealed tube at I40° C. for five hours. The tube opened with pressure , giving off the odor of nitrobenzoyl chloride. On making the acid solution of the tube contents alkaline with NaOH, no base was formed. The benzene solution contained a large quantity of meta-nitrobenzanilid. Melting point, I53° to I54° C.

ANALYSIS OF META-NITROBENZANILID (KJELDAHL).

.I003 gram substance required 8.24 Cc. N/I0 acid.

.II49 gram substance required 9.49 Cc. N/I0 acid.

	Calculated for $C_{I3}H_{I0}O_3N_2$	Found
Nitrogen	II.57	II.50
		II.56

The di-phenyl meta-nitrobenzamidine does not seem to have been made from the literature. The para* compound has been made by treating para-benzoic acid with aniline and two moles of PCl_3 at I80° to I90° C.

The reaction between diphenyl urea and meta-nitrobenzoyl chloride was tried by heating molecular quantities in a large test tube with an outlet tube leading into mercury. HCl and isocyanate could be detected as they bubbled through the mercury during the reaction. The temperature of the oil bath was kept at I70° C. The contents of the tube were treated as before, but the reaction product was meta-nitrobenz-

*Ber. I2,I03.

anilid* obtained in fine, light yellow needles when crystallized from alcohol. Melting point, I53° to I54° C.

DI-PARATOLYLUREA and META NITROBENZOYL CHLORIDE.

20 grams di paratolyl urea and I5.4 grams meta-nitrobenzoyl chloride were heated in a sealed tube at I60° C. for six hours. The contents dissolved in alcohol and then dilute HCl was added. A sticky, brown mass was formed when adding water. Some of the alcohol was evaporated off and NaOH was added to the acid solution. The base formed was recrystallized from alcohol and melted at I36° to I37° C. Its crystals are fine, yellow needles.

ANALYSIS OF BASE FOR NITROGEN (Kjeldahl).

.225I gram base required I9.74 Cc. N/I0 acid.

.2034 gram base required I8.58 Cc. N/I0 acid.

	Calculated for $C_{2I}H_{I9}O_2N_3$	Found
Nitrogen	I2.~~20~~ 18	I2.79 I2.27

A good quantity of meta-nitrobenz-para-toluid was obtained. It crystallizes in fine needles from alcohol. Melting point, I62° C.

This reaction was also tried in a test tube with a lead tube to mercury. HCl and isocyanate were given off freely. The product of the reaction was mostly meta-nitrobenz-para toluid. Melting point, I62° C. A little base was obtained. Melting point, I36° to I37° C. The reaction

evidently had not been completely carried out and only the toluid had been formed.

Several substituted ureas were made during the progress of this work. Their preparation will be briefly mentioned.

METHYL ETHER OF THIOCARBANILID.

This carbanilid and methyl iodide were mixed together in molecular proportions in alcohol and heated on a water bath with a reflux condenser for six hours. The HI salt is formed. On adding Na_2CO_3 solution, the thio urea is formed. The reaction is:

$$\begin{matrix} C_6H_5NH \\ C_6H_5NH \end{matrix}\!\!\diagdown\!\!\diagup C = S + CH_3\,I \rightarrow \begin{matrix} C_6H_5N \\ C_6H_5N \end{matrix}\!\!\diagdown\!\!\diagup H - C - S - CH_3 + HI$$

DI PHENYLMETHYL THIO UREA

Phenyl mustard oil and monomethyl aniline were mixed in molecular quantities and allowed to stand over night. Considerable heat was evolved during the reaction. The crystalline mass formed was recrystallized from alcohol. Melting point, 90° C.

$$C_6H_5NCS + C_6H_5NHCH_3 \rightarrow C_6H_5NHCSN\begin{matrix} CH_3 \\ C_6H_5 \end{matrix}$$

TRI PHENYL METHYL UREA

Molecular quantities of the diphenyl methyl thio urea and di phenyl urea chloride were heated on an oil bath

at I50° C. The product was recrystallized from alcohol. Melting point, I05° C. It was tested for sulphur by the sodium nitroprusside test but no sulphur was formed.

$$C_6H_5HNCSN\begin{matrix}CH_3\\C_6H_5\end{matrix} + \begin{matrix}C_6H_5\\C_6H_5\end{matrix}NCoCl \rightarrow$$

$$\begin{matrix}C_6H_5\\CH_3\end{matrix}N\ C\ O.\ N\begin{matrix}C_6H_5\\C_6H_5\end{matrix} + C_6H_5NCS + HCl$$

ANALYSIS FOR NITROGEN (Kjeldahl).

.I205 gram substance required 8.I3 Cc. N/IO HCl.

.I320 gram substance required 8.95 Cc. N/IO HCl.

	Calculated for $C_{20}H_{18}N_2O$	Found
Nitrogen	9.27	9.45 9.49

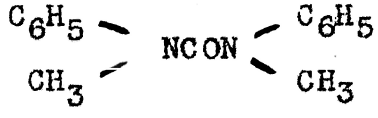
DIPHENYL DI METHYL UREA

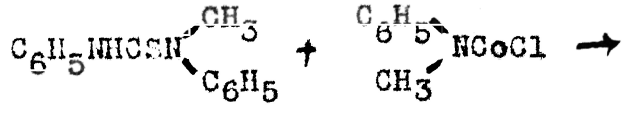
Diphenyl methyl thio urea was also heated with phenyl methyl urea chloride on an oil bath at I50° C. The product was distilled with steam and phenyl mustard oil came over. It was identified by heating it with aniline and HCl. The crystals obtained melted at I5I° C. This corresponds with the melting point of thiocarbanilide. The product left after steam distillation was recrystallized from alcohol and tested for sulphur by sodium nitroprusside. A negative test resulted.

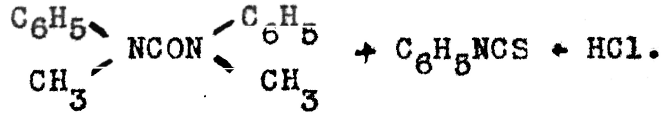
ANALYSIS FOR NITROGEN (Kjeldahl).

.I35I gram substance required II.69 Cc. N/IO HCl.

	Calculated for $C_{15}H_{16}ON_2$	Found.
Nitrogen	II.66	I2.II

The urea was 





In conclusion, I wish to thank Doctor F. B. Dains for his many helpful suggestions during this work.

University of Kansas
May I5th., I9I4.